REMARKS

This Amendment responds to the August 16, 2007 Notice of Non-Compliant Amendment in which the Examiner rejected claims 1-5 and 10-14. Claims 6-9 were withdrawn pursuant to a restriction requirement. In response, applicant has amended the claims herein. Reconsideration and reexamination are respectfully requested in view of the foregoing amendment and the following remark.

The §112 Rejections

Claims 10-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner asks applicants to clarify what is meant by the fractions of A, B, and C and Quil 1-21.

Regarding the definition of fraction A, B and C respectively please refer to the corresponding PCT-description WO 2004/004762, the three last paragraphs on page 6 and the first paragraph on page 7 where it is stated:

The saponin fractions according to the invention may be the A, B, and C fractions described in WO 96/11711, the B3, B4 and B4b fractions described in EP 0 436 620. The fractions QA1-22 described in EP 0 3632 B2, Q-VAC (Nor-Feed, AS Denmark), *Quillaja Saponaria* Molina Spikoside (Isconova AB, Ultunaallen 2B 756 51 Uppsala, Sweden)

The fractions QA-1-2-3-4-5-6-7-8-9-10-11-12-13-14-15-16-17-18-19-20-21 and 22 of EP 0 3632 279 B2, especially QA-7, 17-18 and 21 may be used. They are obtained as described in EP 0 3632 279 B2, especially on page 6 and in Example 1 on page 8 and 9.

Fractions A, B, and C described in WO 96/11711 are prepared from the lipophilic fraction obtained on chromatographic separation of the crude aqueous *Quillaja Saponaria* Molina extract and elution with 70% acetonitrile in water to recover the lipophilic fraction. This lipolhilic fraction is then separated by semipreparative HPLC with elution using a gradient of from 25% to 60% acetonitrile in acidic water. The fraction referred to herein as "Fraction A" or "QH-A" is, or corresponds to, the fraction, which is eluted at approximately 39% acetonitrile. The fraction referred to herein as "Fraction B" or "QH-B" is, or corresponds to, the fraction, which is eluted at approximately 47% acetonitrile. The fraction referred to herein as "Fraction C" or QH-C is, or corresponds to, the fraction, which is eluated at approximately 49% acetonitrile.

The Anticipation Rejections

The Examiner has rejected claim 1-5, and 14 under 35 U.S.C. §102(b) as being anticipated by Nord. The Examiner asserts that applicant's claim is drawn to a composition of at least two iscom complexes from *Quillaja Saponaria* Molina, Quil 1-21, and that Nord teaches saponins from the bark of the *Quillaja Saponaria* Molina tree used as adjuvants with vaccines. The Examiner has also

rejected claims 1-5 under 35 U.S.C. §102(b) as being anticipated by De Vries. The Examiner asserts that applicant's claims are directed to a composition of at least two iscom complexes from *Quillaja Saponaria* Molina, and that De Vries teaches saponin extract from *Quillaja Saponaria* Molina in Quil A. Further, the Examiner has rejected claims 1-5 are rejected under 35 U.S.C. §102(b) as being anticipated by MacFarlan. The Examiner states that applicant's claims and that are for composition of at least two iscom complexes from *Quillaja Saponaria* Molina, MacFarlan teaches saponin from *Quillaja Saponaria*. Similarly, the Examiner rejects claims 1-5 and 10-13 are rejected under 35 U.S.C. §102(b) as being anticipated by Cox. The Examiner states that, applicant's claim same drawn to a composition of at least two iscom complexes from *Quillaja Saponaria* Molina, fractions A, B, C, with 50 to 70% by weight of fraction A, from 30-70% be weight of fraction C. The Examiner asserts that Cox teaches saponin preparation of saponins of *Quillaja Saponaria* from 50 to 90% by weight of Fraction A and from 50 to 10% by weight of Fraction C, 50 to 70% by weight of fraction A and from 50 to 30% by weight of fraction C, and 70% by weight of fraction A, about 30% by weight of fraction C, fractions A, B, and C.

Claims 1-5, 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Kensil. The Examiner states that applicant's claims are for a composition of at least two iscom complexes from *Quillaja Saponaria* Molina, Quil 1-21, and that Kensil teaches Quillaja saponin preparation separated into at least 22 peaks.

Claims 1-5, 10-13 are rejected under 35 U.S.C. 102(b) as being anticipated by the '687 Cox patent. The '697 Cox patent according to the Examiner, teaches a saponin vaccine preparation comprising Quillaja Saponaria from 50% to 70% by weight of Fraction A of Quil A and from 50% to 30% by weight of Fraction C of Quil A.

In response, applicant has requests reconsideration of the rejection. The present invention relates to a composition comprising a mixture of at least two iscom complexes or iscom matrix complexes, each complex comprising one saponin fraction from *Quillaja Saponaria* Molina. The type of saponin fraction is different in the at least two iscom or iscom matrix complexes. It has turned out the compositions have less side effects and are less toxic when different saponins from *Quillaja Saponaria* are integrated into different iscom or Iscom matrix particles.

First, a distinct difference exists between an iscom complex and an iscom matrix complex. An iscom complex is composed of at least one glycoside, at least one lipid, and at least one type of antigen substance. The lipid Is usually a sterol, such as cholesterol, and optionally may be phoslhatidyl choline.

An iscom matrix comprises at least one glycoside and at least one lipid. The lipid is usually a sterol such as cholesterol, and optionally phosphatidyl choline. An iscom matrix complex is most often used in ad mixture with an antigen, whereas the antigen is part of the iscom complex.

Nordet discusses the structures of saponins from *Quillaja Saponaria* within the fraction C. This article does not disclose iscoms or iscom matrices. USP 4,900,549 (de Vries) discusses the production of iscoms with added lipids. Nothing is mentioned about separate saponins or different saponins in different iscom particles. WO 96/36772 (Mac Farlain) describes a method for binding proteins or peptides into iscom matrices with the help of chelating lipids to prepare iscoms. The reference fails to mention that different saponins may be integrated into different iscom particles. WO 96/11711 (Cox) relates to a saponin preparation comprising from 50% to 90% by weight of Fraction A of *Quillaja Saponaria* and from 50% to 10% by weight of Fraction C of Quil A. Even though the reference mentions iscom matrix, it fails to state that different types of saponin fractions may be integrated into different iscom matrix particles, or any of the advantages flowing therefor. EP 0 362 279 dicsloses separation and cleaning of different Quillaja Saponins to be used as adjuvant in free form. Different saponin fractions of *Quillaja Saponaria* are disclosed. No iscom or iscom matrices are mentioned.

Thus, none of the cited publications mentions the integration of different saponin fractions into different complex of iscom or iscom matrix. Applicant submits therefore that the subject anticipation rejection be withdrawn.

The Obviousness Rejections

The Examiner has rejected claims 1-5, 10-14 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Cox. The Examiner states that applicant's claim is for a composition of at least two iscom complexes from *Quillaja Saponaria* Molina, fractions A, B, C, 50 to 70% by weight of fraction A, from 30 to 70% be weight of fraction C.

The Examiner further states that Cox teaches preparation of saponins of Quillaja saponaria from 50 to 90% by weight of Fraction A and from 50 to 10% by weight of Fraction C; 50 to 70% by weight of fraction A and from 50 to 30% by weight of fraction C; about 70% by weight of fraction A; about 30% by weight of fraction C (claims 1-3), fractions A, B, and C. The Examiner admits, however, that Cox does not teach the specific percentage weight claimed, and that the reference also does not specifically teach adding the ingredients in the amounts claimed by applicant. The Examiner contends, however, that the amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize and that optimization of general conditions is a routine practice that would be obvious for a person of ordinary skill in the art to employ. The Examiner states that it would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results. Thus, the Examiner concludes, absent some demonstration of unexpected results from the claimed

parameters, this optimization of ingredients amount would have been obvious at the time of applicant's invention.

As discussed above, the cited references do not disclose or suggest the claimed invention. De Vries discusses iscoms and the importance of adding lipids, but fails to teach or suggest anything about separate saponins or different saponins in different iscom particles. Further, MacFarlan purports to discuss a method for binding proteins or peptides into iscom matrices with the help of chelating lipids to prepare iscoms. The reference is silent on the possibility that different saponins may be integrated into difference iscom particles. Cox (W096/11711) appears to relate to a saponin preparation comprising from 50% to 90% by weight of fraction A of *Quillaja Saponaria* and from 50% to 10% by weight of fraction C of Quil A. Even though the reference appears to mention an iscom matrix, it does not disclose that different types of saponin fractions may be integrated into different iscom matrix particles or that this should bring about any advantages. Likewise, the European application discusses separation and cleaning of different *Quillaja Saponaria* for use in free form as adjuvants. Although different saponin fractions of *Quillaja Saponaria* appear to be disclosed, no iscom or iscom matrices are mentioned.

Thus, none of the cited references mentions the integration of different saponin fractions into different complexes of iscom or iscom matrices, nor are the differences between the cited references and the claimed invention merely a

matter of range optimization. As such, applicants respectfully request that the outstanding obviousness rejection of claims 1-5 and 10-14 be reconsidered and withdrawn.

If any additional fee is required in connection with the filing of the response, the Commissioner is authorized to charge the fee therefor to Deposit Account No. 03-3125. If a further extension of time is deemed required, applicants request such extension, and authorize the fee therefor to be charged to the foregoing deposit account.

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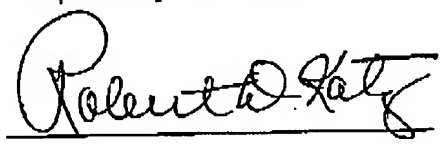
Respectfully submitted,



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